Fig. 1

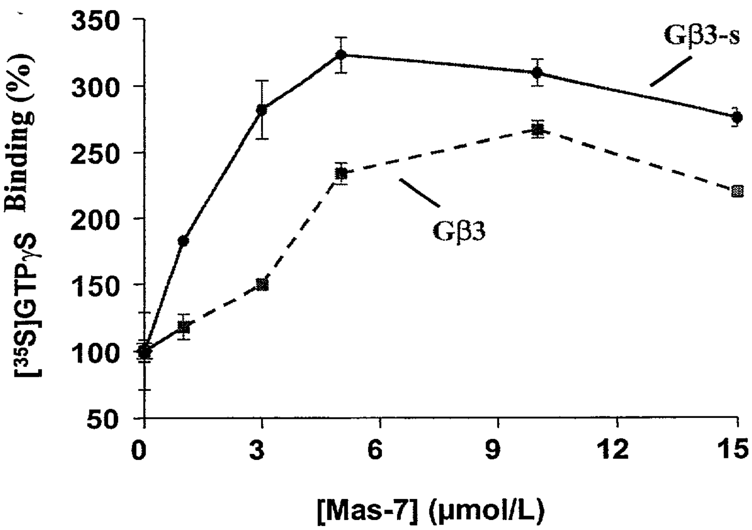

350
300
250
200
150
100
50
[35S]GTPγS Binding (%)
Gβ3-s
Gβ3
0
3
6
9
12
15
[Mas-7] (µmol/L)

Fig. 2

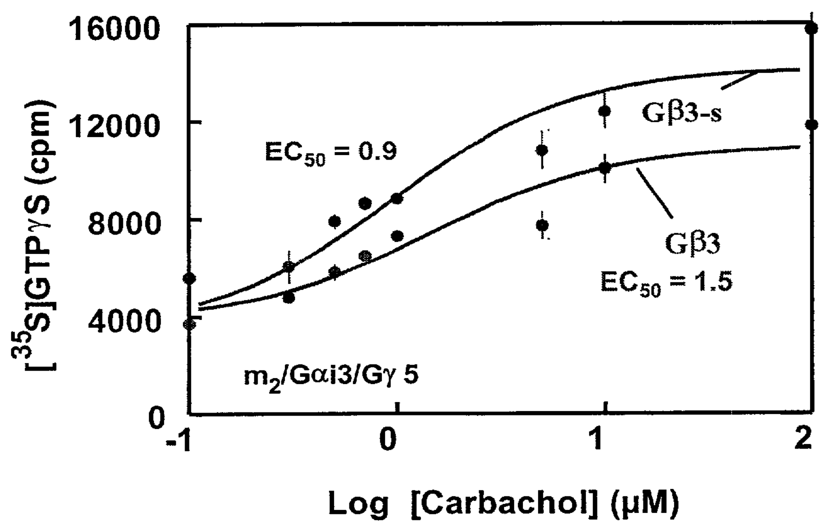

16000
12000
8000
4000
0
[35S]GTPγS (cpm)
EC50 = 0.9
Gβ3-s
Gβ3
EC50 = 1.5
m2/Gαi3/Gγ 5
-1
0
1
2
Log [Carbachol] (μM)

Fig. 3

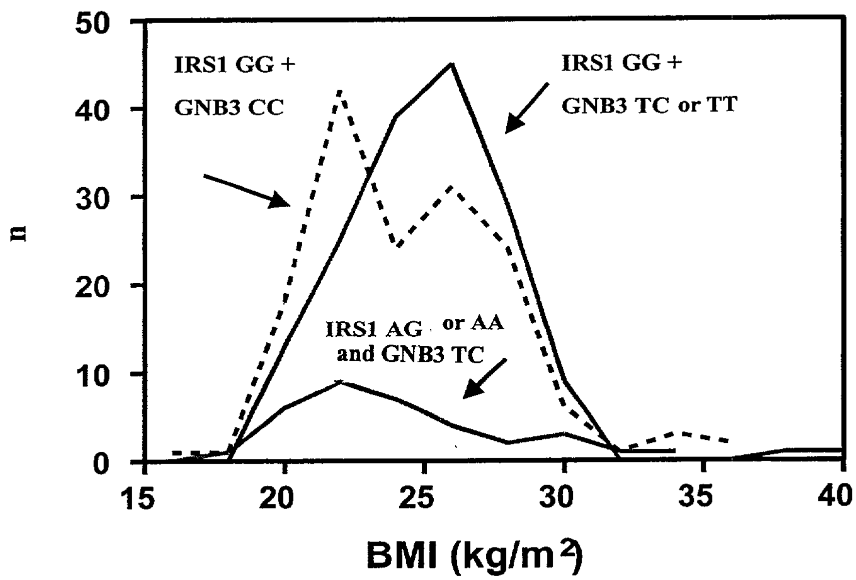

50
40
30
20
10
0
n
15
20
25
30
35
40
BMI (kg/m2)
IRS1 GG +
GNB3 CC
IRS1 GG +
GNB3 TC or TT
IRS1 AG or AA
and GNB3 TC

Fig. 4

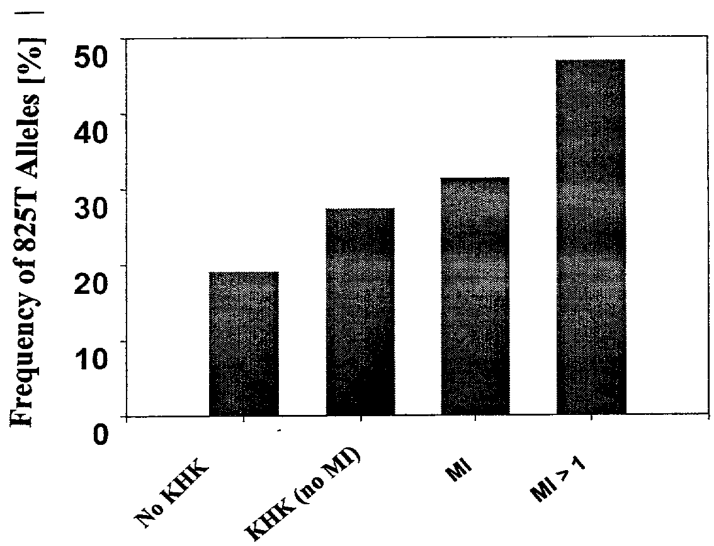

Frequency of 825T Alleles [%]
50
40
30
20
10
0
No KHK
KHK (no MI)
MI
MI > 1

Fig. 5

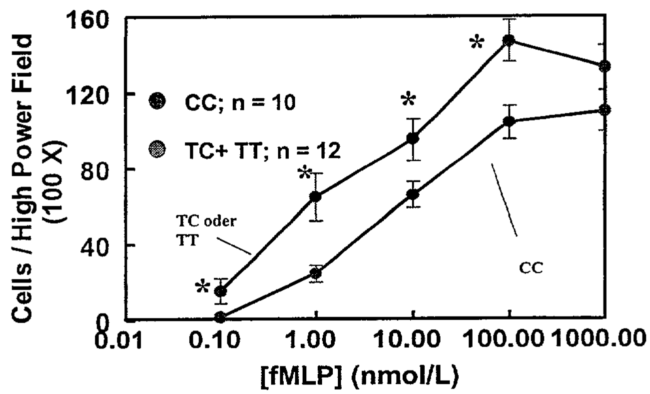

160
120
80
40
0
Cells / High Power Field
(100 X)
CC; n = 10
TC+ TT; n = 12
TC oder
TT
CC
*
*
*
*
0.01
0.10
1.00
10.00
100.00
1000.00
[fMLP] (nmol/L)

Fig. 6

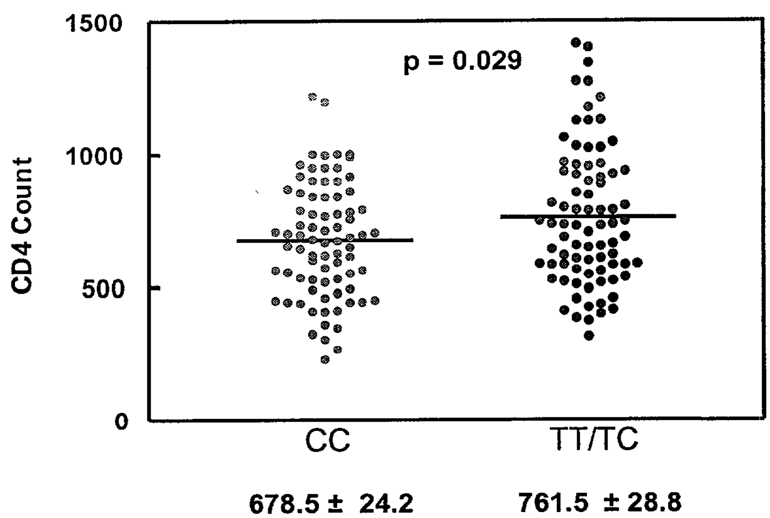


Fig. 7

Enhanced Chemotaxis of T-Lymphocytes from 825T Allele Carriers

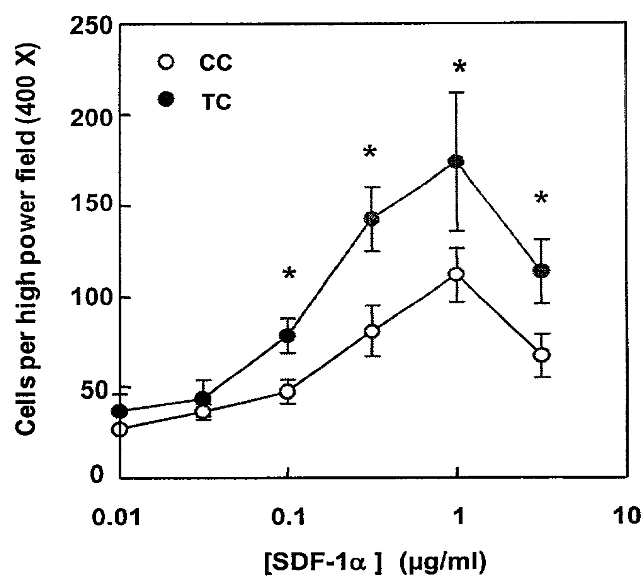


Fig. 8

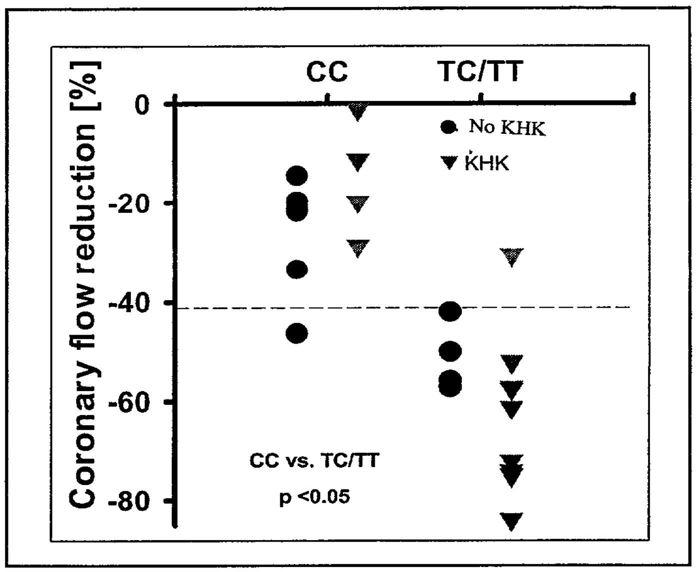

CC
TC/TT
Coronary flow reduction [%]
0
-20
-40
-60
-80
No KHK
KHK
CC vs. TC/TT
p <0.05

Fig. 9

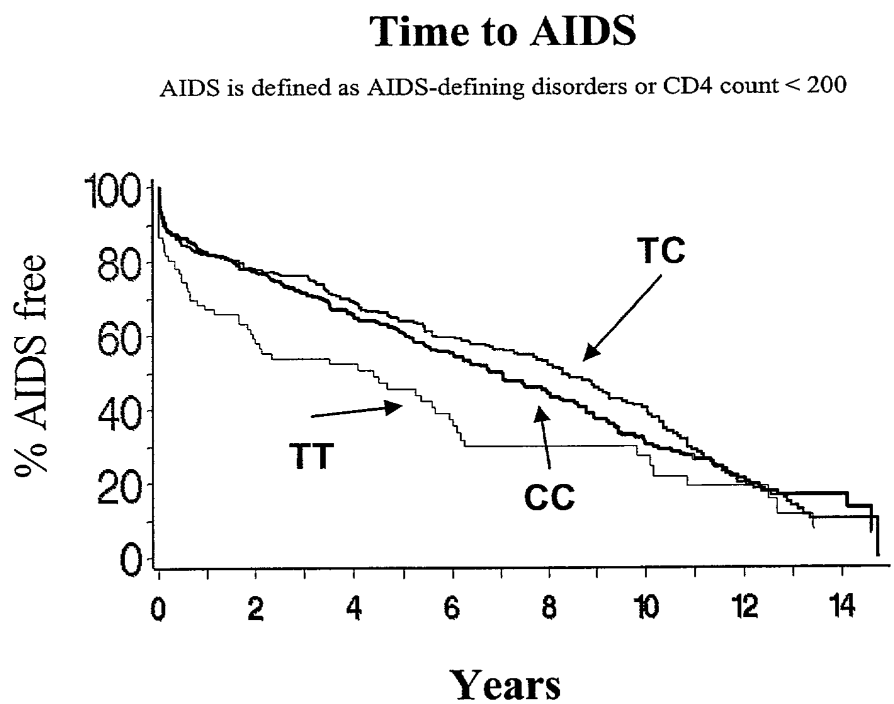

Time to AIDS
AIDS is defined as AIDS-defining disorders or CD4 count < 200
% AIDS free
100
80
60
40
20
0
0
2
4
6
8
10
12
14
Years
TC
TT
CC

Fig. 10

Event: CD4 Cell Count Below 200 per µl

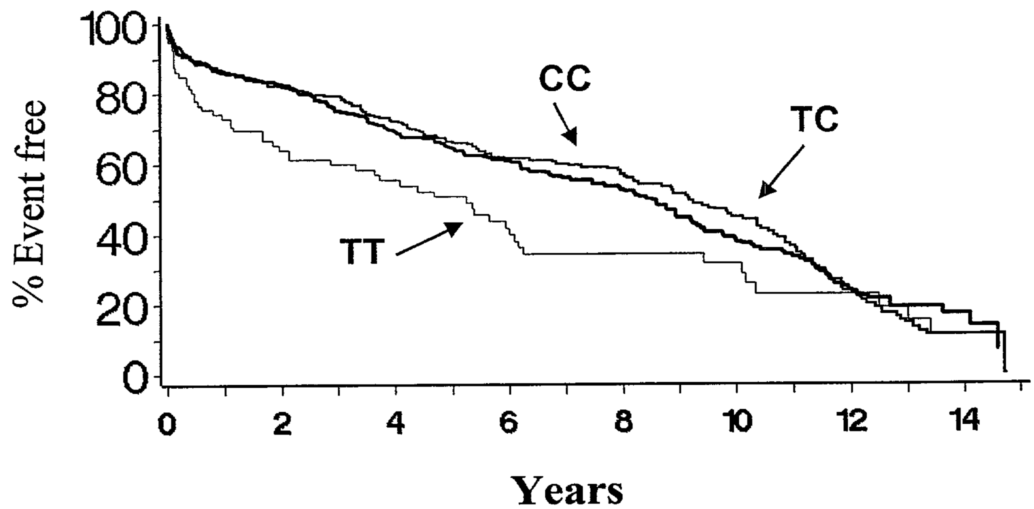


Fig. 11

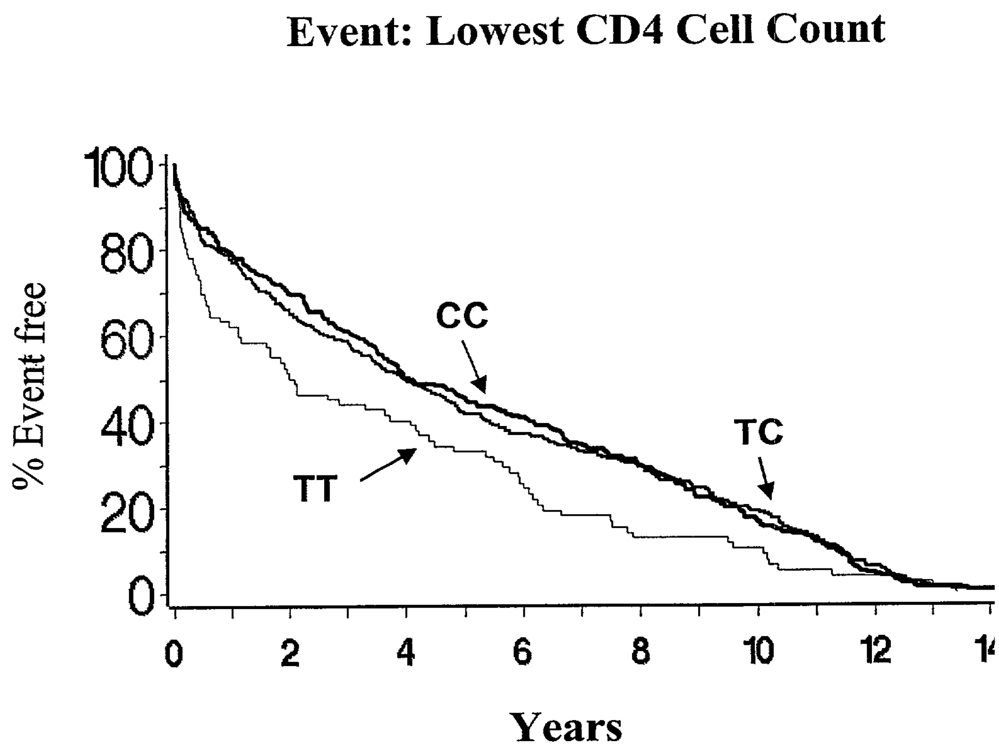

Event: Lowest CD4 Cell Count
% Event free
100
80
60
40
20
0
CC
TC
TT
0
2
4
6
8
10
12
14
Years

Fig. 12

Event: Time to maximum HIV Virus Load

Virus Copy Number determined by Quantitative PCR

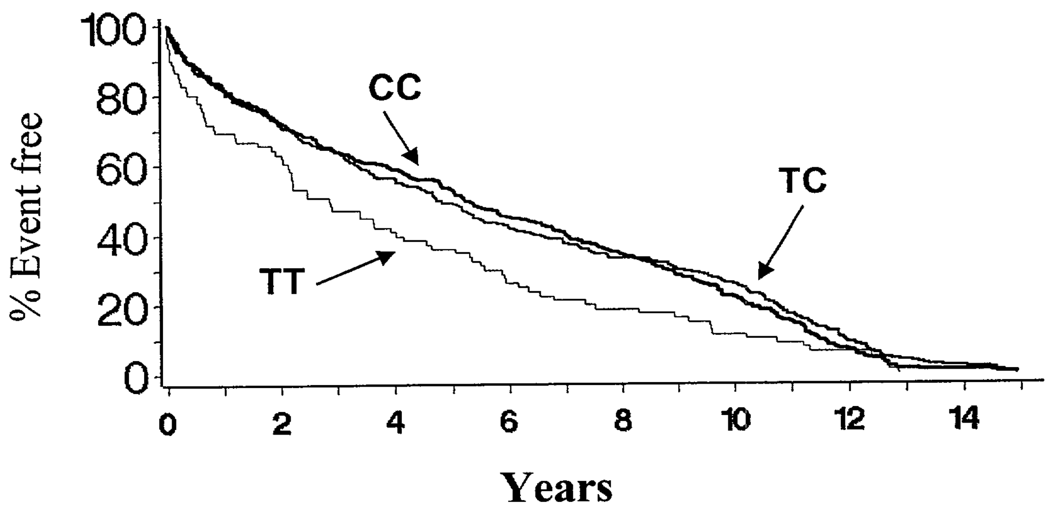


Fig. 13

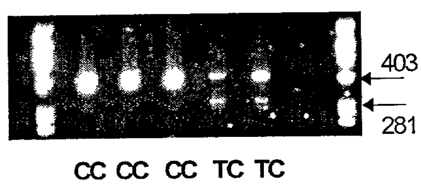
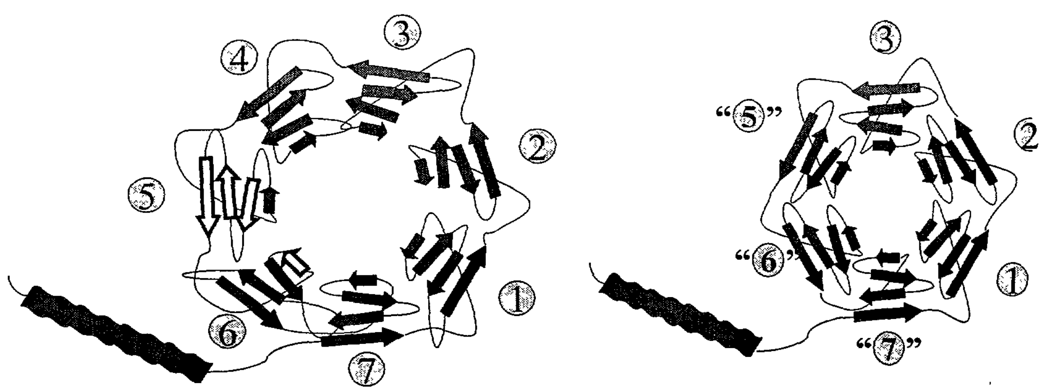


Fig. 14

Potential Structures of Gβ3 and Gβ3s / Gβ3s-2



Gβ3 **Gβ3s-2**

Deletion in Gβ3s-2

Fig. 15

ı Sf9 Cells
varianten

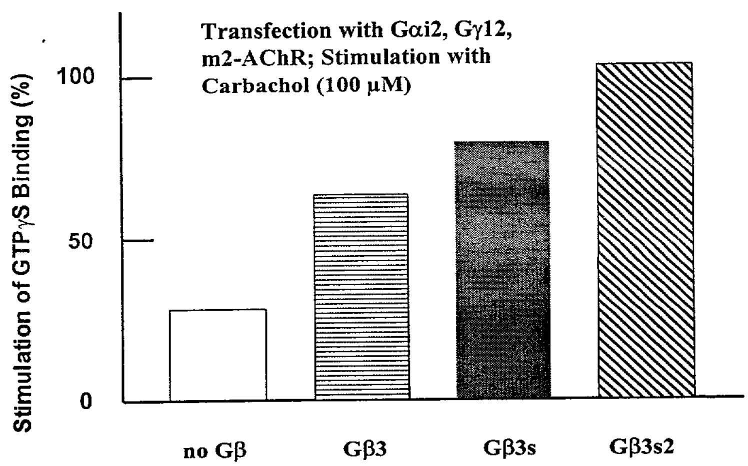


Fig. 16

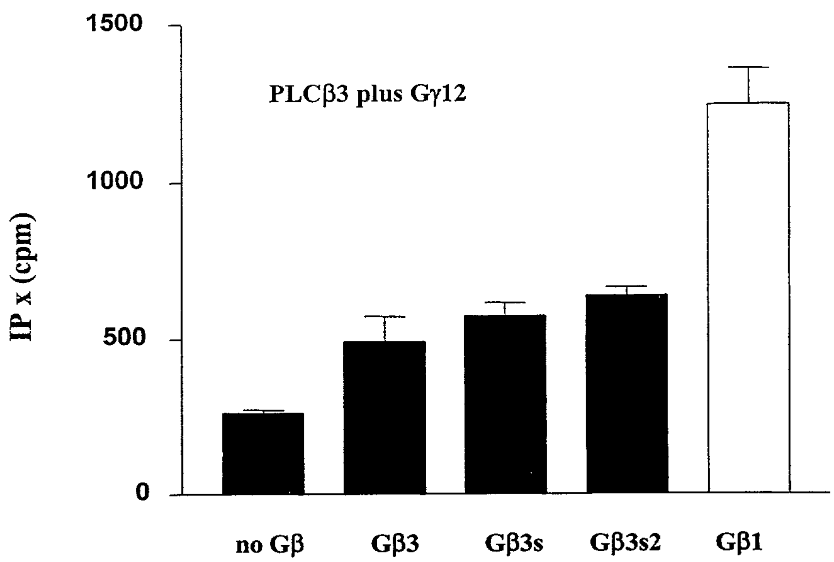

PLCβ3 plus Gγ12
IP x (cpm)
1500
1000
500
0
no Gβ
Gβ3
Gβ3s
Gβ3s2
Gβ1

FIG. 17 ß3-original sequence of Levine. The exons are underlined alternately. The area which is omitted by cryptic splice as bold-faced.

```
1    gggtcgATGG GGGAGATGGA GCAACTGCGT CAGGAAGCGG AGCAGCTCAA GAAGCAGATT
    Start-ATG    EXON 3 after Ansari-Lari
    Nucleotide 1-6 seem not to be affected

61   GCAGATGCCA GGAAAGCCTG TGCTGACGTT ACTCTGGCAG AGCTGGTGTC TGGCCTAGAG
       /Beginning EXON 4                                 /EXON 5 Beginning
                                                         ==> ENDE 1 KLON ANSARI

121  GTGGTGGGAC GAGTCCAGAT GCGGACGCGG CGGACGTTAA GGGGACACCT GGCCAAGATT
       EXON 5

181  TACGCCATGC ACTGGGCCAC TGATTCTAAG CTGCTGGTAA GTGCCTCGCA AGATGGGAAG
       EXON 5                       / Beginning EXON 6

241  CTGATCGTGT GGGACAGCTA CACCACCAAC AAGGTGCACG CCATCCCACT GCGCTCCTCC
       EXON 6                            / EXON 7

301  TGGGTCATGA CCTGTGCCTA TGCCCCATCA GGGAACTTTG TGGCATGTGG GGGGCTGGAC
       EXON 7

361  AACATGTGTT CCATCTACAA CCTCAAATCC CGTGAGGGCA ATGTCAAGGT CAGCCGGGAG
       EXON 7

421  CTTTCTGCTC ACACAGGTTA TCTCTCCTGC TGCCGCTTCC TGGATGACAA CAATATTGTG
       EXON 7        /EXON 8

481  ACCAGCTCGG GGGACACCAC GTGTGCCTTG TGGGACATTG AGACTGGGCA GCAGAAGACT
       EXON 8                /EXON 9

                                     cryptic SPLICING
541  GTATTTGTGG GACACACGGG TGACTGCATG AGCCTGGCTG TGTCTCCTGA CTTCAATCTC
     EXON 9
     cryptic SPLICING

601  TTCATTTCGG GGGCCTGTGA TGCCAGTGCC AAGCTCTGGG ATGTGCGAGA GGGGACCTGC
       EXON 9
         cryptic SPLICING    /

661  CGTCAGACTT TCACTGGCCA CGAGTCGGAC ATCAACGCCA TCTGTTTCTT CCCCAATGGA
       EXON 9                                          / Beginning EXON 10

721  GAGGCCATCT GCACGGGCTC GGATGACGCT TCCTGCCGCT TGTTTGACCT GCGGGCAGAC
       EXON 10

781  CAGGAGCTGA TCTGCTTCTC CCACGAGAGC ATCATCTGCG GCATCACGTC CGTGGCCTTC
       EXON 10       Polymorphism site               acgtc tgt

841  TCCCTCAGTG GCCGCCTACT ATTCGCTGGC TACGACGACT TCAACTGCAA TGTCTGGGAC
       EXON 10

901  TCCATGAAGT CTGAGCGTGT GGGCATCCTC TCTGGCCACG ATAACAGGGT GAGCTGCCTG
       EXON 10            /Beginning EXON 11

961  GGAGTCACAG CTGACGGGAT GGCTGTGGCC ACAGGTTCCT GGGACAGCTT CCTCAAAATC
       EXON 11

1021 TGGAACTGAg gaggctggag aaagggaagt ggaaggcagt gaacacactc agcagccccc
       EXON 11
               End of Open Reading Frame

1081 tgcccgaccc catctcattc aggtgttctc ttctatattc cgggtgccat tcccactaag
       EXON 11

1141 ctttctcctt tgagggcagt ggggagcatg ggactgtgcc tttgggaggc agcatcaggg
       EXON 11
```

1201 acacaggggc aaagaactgc cccatctcct cccatggcct tccctcccca cagtcctcac
EXON 11

1261 agcctctccc ttaatgagca aggacaacct gcccctcccc agccctttgc aggcccagca
EXON 11

1321 gacttgagtc tgaggcccca ggccctagga ttcctccccc agagccacta cctttgtcca
EXON 11

"Ban Polymorphismus"
tctggcacta cta

1381 ggcctgggtg gtatagggcg tttggccctg tgactatggc tctggcacca ctagggtcct
EXON 11

1441 ggccctcttc ttattcatgc tttctccttt ttctaccttt ttttctctcc taagacacct
EXON 11

1501 gcaataaagt gtagcacccct ggt
EXON 11 POLY A SITE

Fig. 18 Sequence with two polymorphisms (Numbering after the Levine sequence)

```
gggtcgatgg gggagatgga gcaactgcgt caggaagcgg agcagctcaa gaagcagatt     60
gcagatgcca ggaaagcctg tgctgacgtt actctggcag agctggtgtc tggcctagag    120
gtggtgggac gagtccagat gcggacgcgg cggacgttaa ggggacacct ggccaagatt    180
tacgccatgc actgggccac tgattctaag ctgctggtaa gtgcctcgca agatgggaag    240
ctgatcgtgt gggacagcta caccaccaac aaggtgcacg ccatcccact gcgctcctcc    300
tgggtcatga cctgtgccta tgccccatca gggaactttg tggcatgtgg ggggctggac    360
aacatgtgtt ccatctacaa cctcaaatcc cgtgagggca atgtcaaggt cagccgggag    420
ctttctgctc acacaggtta tctctcctgc tgccgcttcc tggatgacaa caatattgtg    480
accagctcgg gggacaccac gtgtgccttg tgggacattg agactgggca gcagaagact    540
gtatttgtgg gacacacggg tgactgcatg agcctggctg tgtctcctga cttcaatctc    600
ttcatttcgg gggcctgtga tgccagtgcc aagctctggg atgtgcgaga ggggacctgc    660
cgtcagactt tcactggcca cgagtcggac atcaacgcca tctgtttctt ccccaatgga    720
gaggccatct gcacgggctc ggatgacgct tcctgccgct tgtttgacct gcgggcagac    780
caggagctga tctgcttctc ccacgagagc atcatctgcg gcatcacgtc tgtggccttc    840
tccctcagtg gccgcctact attcgctggc tacgacgact tcaactgcaa tgtctgggac    900
tccatgaagt ctgagcgtgt gggcatcctc tctggccacg ataacagggt gagctgcctg    960
ggagtcacag ctgacgggat ggctgtggcc acaggttcct gggacagctt cctcaaaatc   1020
tggaactgag gaggctggag aaagggaagt ggaaggcagt gaacacactc agcagccccc   1080
tgcccgaccc catctcattc aggtgttctc ttctatattc cgggtgccat tcccactaag   1140
ctttctcctt tgagggcagt ggggagcatg ggactgtgcc tttgggaggc agcatcaggg   1200
acacaggggc aaagaactgc cccatctcct cccatggcct tccctcccca cagtcctcac   1260
agcctctccc ttaatgagca aggacaacct gcccctcccc agccctttgc aggcccagca   1320
gacttgagtc tgaggcccca ggccctagga ttcctccccc agagccacta cctttgtcca   1380
tctggcacta ctaggcctgg gtggtatagg gcgtttggcc ctgtgactat ggctctggca   1440
ccactagggt cctggccctc ttcttattca tgctttctcc tttttctacc tttttttctc   1500
tcctaagaca cctgcaataa agtgtagcac cctggt                             1536
```

Fig. 19 Nucleic acid sequence of cDNA of Gß3 and description of the deletion in Gß3 and Gß3s-2. Numbering referenced to the cDNA of Levine et al.(Levine, M.A., Smallwood, P.M., Moen, P.T.,Jr., Helman, L.J., and Ahn, T.G. Molecular cloning of ß3 subunit, a third form of the G protein beta-subunit polypeptide. *Proc.Natl.Acad.Sci.USA* 87(6):2329-2333, 1990) Here numbering does not begin with start codon ATG, but 6 nucleotides earlier in the 5' area.

```
1     gggtcgATGG GGGAGATGGA GCAACTGCGT CAGGAAGCGG AGCAGCTCAA GAAGCAGATT
     Start-ATG    EXON 3
     Nucleotide 1-6 seem not to be affected

61    GCAGATGCCA GGAAAGCCTG TGCTGACGTT ACTCTGGCAG AGCTGGTGTC TGGCCTAGAG
        /Beginn EXON 4                                /EXON 5 Beginning

121   GTGGTGGGAC GAGTCCAGAT GCGGACGCGG CGGACGTTAA GGGGACACCT GGCCAAGATT
       EXON 5

181   TACGCCATGC ACTGGGCCAC TGATTCTAAG CTGCTGGTAA GTGCCTCGCA AGATGGGAAG
       EXON 5                        / Beginning EXON 6

241   CTGATCGTGT GGGACAGCTA CACCACCAAC AAGGTGCACG CCATCCCACT GCGCTCCTCC
       EXON 6                             / EXON 7

301   TGGGTCATGA CCTGTGCCTA TGCCCCATCA GGGAACTTTG TGGCATGTGG GGGGCTGGAC
       EXON 7

361   AACATGTGTT CCATCTACAA CCTCAAATCC CGTGAGGGCA ATGTCAAGGT CAGCCGGGAG
       EXON 7

421   CTTTCTGCTC ACACAGGTTA TCTCTCCTGC TGCCGCTTCC TGGATGACAA CAATATTGTG
       EXON 7          /EXON 8
```

```
                                    Deletion bei Gβ3s
481   ACCAGCTCGG GGGACACCAC GTGTGCCTTG TGGGACATTG AGACTGGGCA GCAGAAGACT
        EXON 8                 /EXON 9

541   GTATTTGTGG GACACACGGG TGACTGCATG AGCCTGGCTG TGTCTCCTGA CTTCAATCTC
        EXON 9

601   TTCATTTCGG GGGCCTGTGA TGGCAGTGCC AAGCTCTGGG ATGTGCGAGA GGGGACCTGC
        EXON 9

                                                         Deletion in Gβ3s2
661   CGTCAGACTT TCACTGGCCA CGAGTCGGAC ATCAACGCCA TCTGTTTCTT CCCCAATGGA
        EXON 9                                          / Beginn EXON 10
                                                  Intron dazwischen 1607 bp

      Deletion in Gβ3s2
721   GAGGCCATCT GCACGGGCTC GGATGACGCT TCCTGCCGCT TGTTTGACCT GCGGGCAGAC
        EXON 10

781   CAGGAGCTGA TCTGCTTCTC CCACGAGAGC ATCATCTGCG GCATCACGTC CGTGGCCTTC
        EXON 10                        polymorphism site    acgtc tgt

841   TCCCTCAGTG GCCGCCTACT ATTCGCTGGC TACGACGACT TCAACTGCAA TGTCTGGGAC
        EXON 10

901   TCCATGAAGT CTGAGCGTGT GGGCATCCTC TCTGGCCACG ATAACAGGGT GAGCTGCCTG
        EXON 10               /Beginning EXON 11 (Intron dazw. 989 bp)

961   GGAGTCACAG CTGACGGGAT GGCTGTGGCC ACAGGTTCCT GGGACAGCTT CCTCAAAATC
        EXON 11

1021  TGGAACTGAg gaggctggag aaagggaagt ggaaggcagt gaacacactc agcagccccc
        EXON 11
                End of Open Reading Frame B3-3

1081  tgcccgaccc catctcattc aggtgttctc ttctatattc cgggtgccat tcccactaag
        EXON 11
```

1141 ctttctcctt tgagggcagt ggggagcatg ggactgtgcc tttgggaggc agcatcaggg

EXON 11

1201 acacaggggc aaagaactgc cccatctcct cccatggcct tccctcccca cagtcctcac

EXON 11

1261 agcctctccc ttaatgagca aggacaacct gcccctcccc agccctttgc aggcccagca

EXON 11

1321 gacttgagtc tgaggcccca ggccctagga ttcctccccc agagccacta cctttgtcca

EXON 11

C1423T

tctggcacta cta

1381 ggcctgggtg gtatagggcg tttggccctg tgactatggc tctggcacca ctagggtcct

EXON 11

1441 ggccctcttc ttattcatgc tttctccttt ttctaccttt ttttctctcc taagacacct

EXON 11

1501 gcaataaagt gtagcaccct ggt

EXON 11 POLY A SITE

FIG. 20 Amino acid sequence of Gß3s-2 (Combined production)

```
atg ggg gag atg gag caa ctg cgt cag gaa gcg gag cag ctc aag aag   48
Met Gly Glu Met Glu Gln Leu Arg Gln Glu Ala Glu Gln Leu Lys Lys
                 5                  10                  15

cag att gca gat gcc agg aaa gcc tgt gct gac gtt act ctg gca gag   96
Gln Ile Ala Asp Ala Arg Lys Ala Cys Ala Asp Val Thr Leu Ala Glu
             20                  25                  30

ctg gtg tct ggc cta gag gtg gtg gga cga gtc cag atg cgg acg cgg  144
Leu Val Ser Gly Leu Glu Val Val Gly Arg Val Gln Met Arg Thr Arg
         35                  40                  45

cgg acg tta agg gga cac ctg gcc aag att tac gcc atg cac tgg gcc  192
Arg Thr Leu Arg Gly His Leu Ala Lys Ile Tyr Ala Met His Trp Ala
     50                  55                  60

act gat tct aag ctg ctg gta agt gcc tcg caa gat ggg aag ctg atc  240
Thr Asp Ser Lys Leu Leu Val Ser Ala Ser Gln Asp Gly Lys Leu Ile
65                  70                  75                  75

gtg tgg gac agc tac acc acc aac aag gtg cac gcc atc cca ctg cgc  288
Val Trp Asp Ser Tyr Thr Thr Asn Lys Val His Ala Ile Pro Leu Arg
                 80                  85                  90

tcc tcc tgg gtc atg acc tgt gcc tat gcc cca tca ggg aac ttt gtg  336
Ser Ser Trp Val Met Thr Cys Ala Tyr Ala Pro Ser Gly Asn Phe Val
             95                 100                 105

gca tgt ggg ggg ctg gac aac atg tgt tcc atc tac aac ctc aaa tcc  384
Ala Cys Gly Gly Leu Asp Asn Met Cys Ser Ile Tyr Asn Leu Lys Ser
        110                 115                 120

cgt gag ggc aat gtc aag gtc agc cgg gag ctt tct gct cac aca ggt  432
Arg Glu Gly Asn Val Lys Val Ser Arg Glu Leu Ser Ala His Thr Gly
    125                 130                 135

tat ctc tcc tgc tgc cgc ttc ctg gat gac aac aat att gtg acc agc  480
Tyr Leu Ser Cys Cys Arg Phe Leu Asp Asp Asn Asn Ile Val Thr Ser
140                 145                 150                 155

tcg ggg gac acc acg tgt gcc ttg tgg gac att gag act ggg cag cag  528
Ser Gly Asp Thr Thr Cys Ala Leu Trp Asp Ile Glu Thr Gly Gln Gln
160                 165                 170                 175

aag act gta ttt gtg gga cac acg ggt gac tgc atg agc ctg gct gtg  576
Lys Thr Val Phe Val Gly His Thr Gly Asp Cys Met Ser Leu Ala Val
                180                 185                 190

tct cct gac ttc aat ctc ttc att tcg ggg gcc tgt gat gcc agt gcc  624
ser Pro Asp Phe Asn Leu Phe Ile Ser Gly Ala Cys Asp Ala Ser Ala
            195                 200                 205
```

```
aag ctc tgg gat gtg cga gag ggg acc tgc cgt cag act ttc act ggc     672
Lys Leu Trp Asp Val Arg Glu Gly Thr Cys Arg Gln Thr Phe Thr Gly
        210                 215                 220

cag gag tcg gac atc aac gcc atc tgt ttc ttc tcc ctc agt ggc cgc     720
His Glu Ser Asp Ile Asn Ala Ile Cys Phe Phe Ser Leu Ser Gly Arg
    225                 230                 235

cta cta ttc gct ggc tac gac gac ttc aac tgc aat gtc tgg gac tcc     768
Leu Leu Phe Ala Gly Tyr Asp Asp Phe Asn Cys Asn Val Trp Asp Ser
240                 245                 250                 255

atg aag tct gag cgt gtg ggc atc ctc tct ggc cac gat aac agg gtg     816
Met Lys Ser Glu Arg Val Gly Ile Leu Ser Gly His Asp Asn Arg Val
            260                 265                 270

agc tgc ctg gga gtc aca gct gac ggg atg gct gtg gcc aca ggt tcc     864
Ser Cys Leu Gly Val Thr Ala Asp Gly Met Ala Val Ala Thr Gly Ser
        275                 280                 285

tgg gac agc ttc ctc aaa atc tgg aac tga                             894
Trp Asp Ser Phe Leu Lys Ile Trp Asn ***
    290                 295
```